

REMARKS

Claims 1-9 and 11-21 were pending in this application. Independent claims 1, 5 and 8 have been amended to incorporate the limitation of a retrovirus vector recited in dependent claims 3, 7 and 9, respectively. Accordingly, claims 2-3, 6-7 and 9 have been canceled. Hence, claims 1, 4-5, 8 and 11-21 will be pending upon the entry of this amendment. No new matter has been introduced. The foregoing amendments and claim cancelations are all made without admission and without prejudice to Applicants' right to pursue any subject matter that may be surrendered by those amendments/cancelations in either this or other (e.g., related divisional and/or other continuing) applications. Entry and consideration of these amendments are respectfully requested.

The Rejection(s) Under 35 U.S.C. § 102

Should Be Withdrawn:

Claims 1-4, 4-6, 8 and 11-21 have been rejected under 35 U.S.C. § 102(b), as anticipated by the publication of Kiss *et al.*, "High Throughput Ion-Channel Pharmacology: Planar-Arrya-Based Voltage Clamp" *Assay and Drug Development Technologies* (2003) 1:127-135 (hereinafter referred to as "Kiss"). According to the Office Action, Kiss describes high-throughput patch clamping experiments using cells transformed with a pcDNA3.1 vector to express hERG. The Office Action also argues, citing to Figures 1-2 in Kiss, that the cells have a current greater than 0.6 nA and a success rate greater than 79%.

In response, Applicants respectfully submit that the Examiner has mischaracterized the teachings of Kiss, and that the rejection for anticipation over that publication should be withdrawn. Although Kiss may report at "79 ± 3% success rate" in the right-hand column on page 130, this figure does not describe the proportion of cells with a current greater than 0.6 nA; it simply refers to the number of cells used in Kiss's final data analysis. This is apparent upon a more thorough review of Kiss. In particular, Kiss teaches that its patch clamp measurements are done using a "PatchPlateTM" with 384 measurement wells, each of which holds a single cell for patch-clamp measurement. See Kiss at page 129, left-hand column. Kiss then goes on to state

that "Six PatchPlates were used in this study." *Id.*at 130, left-hand column. Hence, Kiss performed patch-clamp measurements using $6 \times 834 = 2304$ cells. However, Kiss reports that measurements from some of these cells were excluded for various reasons, and that "[i]n all, 1828 cells were used for the final analysis, giving a 79 3% success rate." Hence, Kiss's "success rate" refers to the number of patch-clamp measurements he was able to make and use in his final data analysis: 1828 out of 2314 cells, or $1828/2314 = 79\%$.

Indeed, contrary to what is stated in the Office Action, the cells in Kiss's experiments do not exhibit hERG currents of 0.6 nA or more. Rather, Kiss reports that "[t]he mean peak hERG tail current amplitude was 413 ± 4 pA." Kiss at page 130, right-hand column. This is also apparent from Figure 2C on page 130 of Kiss, which plots the peak hERG current for each of his 1,828 individual patch-clamped cells. It is readily apparent from this plot that fewer than 40% of those cells have an hERG current of 0.6 nA or higher as called for in the pending claims.

For these reasons alone, Kiss does describe or suggest all the limitations of the currently pending claims, and therefore can not anticipate those claims. Moreover, however, Applicants note that the pending independent claims (*i.e.*, claims 1, 5 and 8) have been amended, *supra*, to specify that the cells are transformed with a retroviral vector. The Office Action acknowledges that Kiss does not describe this limitation. See in the Office Action on page 3, Para. 3. For this additional reason, the independent claims as amended, *supra*, can not be anticipated by Kiss. The remaining claims (*i.e.*, claims 4 and 11-21) all depend either directly or indirectly from the amended independent claims, and therefore incorporate their limitations. Hence, these claims also are not anticipated by Kiss. Applicants therefore respectfully submit that the rejection for anticipation over that reference should be withdrawn.

**The Rejection(s) Under 35 U.S.C. § 103(a)
Should Be Withdrawn:**

In addition to rejecting claims 1-2, 4-6, 8 and 11-21 as anticipated, all of the pending claims (*i.e.*, all of claims 1-9 and 11-21) have been rejected under 35 U.S.C. § 103(a) as unpatentable over Kiss in view of the publication by Morgenstern & Land, "Advanced mammalian gene transfer: high titre retroviral vectors with multiple drug selection markers and a

complementary helper-free packaging cell line," *Nucleic Acids Research* (1990) 18(12)3587-3596 (hereinafter referred to as "Morgenstern"). In particular, the Office Action argues that it would have been obvious to use a retroviral vector as described by Morgenstern, to obtain hERG channel expressing cells as described by Kiss. However, and as discussed in detail above, the Kiss publication does not describe a population of hERG expressing cells, where 40% or more of the total hERG transformed cells with an hERG current of 0.6 nA or more. At best, Morgenstern only describes a retroviral vector that might be used, generally, to express exogenous genes in mammalian cells (*see* Morgenstern in the Abstract). Morgenstern says nothing about using this vector to express hERG or any other ion-channel. Even if a skilled person were to use Morgenstern's retroviral vector to express hERG, he would only expect, at best, a population of cells with a similar hERG current as Kiss; (s)he would not believe or expect any difference improvement using the the pcDNA.1neo vector of Kiss. As explained above, however, the hERG current exhibited by Kiss's cells is substantially lower than the 0.6 nA called for in the currently pending claims. A skilled person could not have reasonably expected this from Kiss, even given the teachings of Morgenstern. Hence, the pending claims also are not obvious over those publications.

Conclusion:

For all of the foregoing reasons, Applicants respectfully submit that the rejections unde 35 U.S.C. §§ 102 and 103 have been obviated, and should be withdrawn. The pending claims are not anticipated by Kiss, and they are not obvious over the Kiss publication even in view of the teachings in Morgenstern. There being no other objections or rejections, Applicants respectfully submit that the pending claims are now in condition for allowance. However, the Examiner is invited to contact Applicants' undersigned representative should he believe that

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there is any remaining issue that might be resolved, *e.g.*, by an Examiner's Amendment or by a Supplemental Amendment by Applicants. An allowance is earnestly sought.

Respectfully submitted,

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/Samuel S. Woodley/

CUSTOMER NO.: 26211

Samuel S. Woodley, Ph.D. (Reg. No. 43,287)
Fish & Richardson P.C.
P.O. Box 1022
Minneapolis, MN 55440-1022
Tel. (212) 765-5070
Fax (877) 769-7945
E-mail APSI@FR.COM
Attorneys/Agents for Applicant

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